

AMENDMENTS TO THE SPECIFICATION:

Amend the specification as follows:

Delete the paragraph spanning pages 16-17 and insert the following therefor:

Figure 17: Figure 17 on the left shows by RIA of PTHrP that the production of PTHrP is decreased by 50 % in the 786-0 cells which have been transfected with the vector encoding VHL (786-0 VHL) in comparison with the cells that have not been transfected (786-0 wt) or transfected with the vector alone (786-0 V). Figure ~~[[14]]~~17 on the right shows the secretion of PTHrP in pM per 24 hrs and per million cells.

Delete the paragraph spanning lines 19-27 of page 19 and insert the following therefor:

0.4 mM dNTP, 2.5 U ~~[[RedTaq]]~~REDTAQ DNA polymerase (Sigma) and 0.5 µg (PTHrP) or 1 µg (RPTH1) cDNA. PCR begins with denaturation at 95°C for 4 min, then the cycles are programmed in the following way: 1 min at 94°C (denaturation), 1 min at 60°C (annealing) and 1 min at 72°C (synthesis). PCR is launched for 30 cycles for PTHrP and RPTH1. The last cycle is followed by an additional extension of 8 min at 72°C. The PCR products are separated by electrophoresis on agarose gel at 2% in the presence of 0.5 µg/ml ethidium bromide. The intensity of the bands obtained after electrophoresis is quantified by gel analysis software (SigmaScanPro 4.01, Jandel Scientific, Erkrath, Germany).

Delete the paragraph spanning pages 20-21 and insert the following therefor:

Transfection protocol. The 786-0 cells were cultured in 75cm² culture vessels in the RPMI 1640 medium (cf above) supplemented by 10% serum up to 50% confluence. The adherent cells were then washed 3 times with 10 ml of medium without serum and then maintained in 5 ml of this same medium. In order to transfect the cells, 5 µg of plasmidic DNA (pCR3.1-Uni alone or pCR3.1-Uni VHL) in 50 µl water were incubated with 50 µl [[lipofectamin]] LIPOFECTAMIN (Invitrogen Sarl) at 2 mg/ml for 30 mins at room temperature. This solution is added drop by drop to the cells, then the containers are incubated for 4 hrs at 37°C. After this incubation period, 10 ml of RPMI 1640 medium supplemented by 10% serum were added to the cells. After 24 hrs, the medium is replaced by fresh medium containing 10% serum. Two days later, the medium is replaced by a medium supplemented by 10% FBS and containing 500 µg/ml G418 (neomycin) in order to select the transfected cells. The optimum concentration of G418 was determined for the 786-0 cells by a "death curve" over 3 weeks with concentrations of 25 to 1000 µg/ml of G418 and change of medium every 3 days. For each transfection (vector alone or pCR3.1-Uni VHL), 3 clones were selected as well as all clones (all the clones brought together) and maintained in the RPMI 1640 medium with serum and supplemented by 500 µg/ml G418.

Delete the paragraph spanning lines 16-19 on page 30 and insert the following therefor:

- Figure 13 shows the growth of the tumours of the mice treated either as a control or by the antagonist according to the experimental protocol described above.

The growth results are expressed as a percentage in relation to day 0 of the start of ~~the~~ treatments.

Delete the paragraph spanning lines 15-16 on page 31 and insert the following therefor:

signifies $p < 0.01$ for the growth of ~~the~~ tumours of the mice treated as a control in comparison to day 0 of treatment

Delete the paragraph spanning lines 1-10 on page 32 and insert the following therefor:

- In Figure 15 shown on the left the pCR3.1-Uni vectors, alone or coding for VHL(1-213). These vectors have been transfected in the 786-0 cells (cf above.). Three individual clones were isolated after selection by G418 as well as all of ~~the~~ clones for the transfected cells by the vector alone (786-0 V, individual clones 2, 3, 4 and mixed clones p) or by the coding vector for VHL (786-0 VHL, individual clones 2 3 and 6 and mixed clones p). Parallel to these clones, 3 samples of non-transfected 786-0 cells (786-0 wt for wild-type) and 3 samples of HK-2 cells (normal human proximal tubular cells) were also tested for the expression of VHL and of PTHrP.